

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

Please replace the "Related Applications" section of the specification at page 1, line 5 to page 2, line 2 with the following replacement section:

--- This application claims priority to prior filed U.S. Provisional Application Serial No. 60/397,275, filed July 19, 2002. This application also claims priority to prior filed to U.S. Provisional Application Serial No. 60/411,081, filed September 16, 2002, and prior-filed U.S. Provisional Application Serial No. 60/417490, filed October 10, 2002. This application also claims priority to prior filed to U.S. Provisional Application Serial No. 60/455777, filed March 18, 2003. In addition, this application is related to U.S. Patent Nos. 6,090,382, 6,258,562, and 6,509,015 and 7,223,394. This application is also related to ~~U.S. Patent Application Serial No. 09/801,185, filed March 7, 2001;~~ U.S. Patent Application Serial No. 10/302,356, filed November 22, 2002 (now abandoned); U.S. Patent Application Serial No. 10/163657, filed June 2, 2002; and U.S. Patent Application Serial No. 10/133715, filed April 26, 2002 (now abandoned).

This application is related to U.S. utility applications 10/623039 entitled "Treatment of Spondyloarthropathies Using TNF α Inhibitors," 10/623076 entitled "Treatment of Pulmonary Disorders Using TNF α Inhibitors," 10/623065 (now abandoned) entitled "Treatment of Coronary Disorders Using TNF α Inhibitors," 10/622928 (now abandoned) entitled "Treatment of Metabolic Disorders Using TNF α Inhibitors," 10/623075 entitled "Treatment of Anemia Using TNF α Inhibitors," 10/623035 (now abandoned) entitled "Treatment of Pain Using TNF α Inhibitors," 10/622683 (now abandoned) entitled "Treatment of Hepatic Disorders Using TNF α Inhibitors," 10/622205 (now abandoned) entitled "Treatment of Skin and Nail Disorders Using TNF α Inhibitors," 10/622210 (now abandoned) entitled "Treatment of Vasculitides Using TNF α Inhibitors," 10/623318 entitled "Treatment of TNF α -Related Disorders Using TNF α Inhibitors," and PCT application PCT/US2003/022566 entitled "Treatment of TNF α -Related Disorders," all of which are filed on even date herewith. The entire contents of each of these patents and patent applications are hereby incorporated herein by reference.

Please replace three consecutive paragraphs of the "Detailed Description of the Invention", which begin on page 6, line 20, and end on page 8, line 17 of the specification, with the following amended paragraphs:

--- The term "TNF α inhibitor" includes agents which inhibit TNF α . Examples of TNF α inhibitors include etanercept (Enbrel[®], Amgen), infliximab (Remicade[®], Johnson and Johnson), human anti-TNF monoclonal antibody (D2E7/HUMIRA[®], Abbott Laboratories), CDP 571 (Celltech), and CDP 870 (Celltech) and other compounds which inhibit TNF α activity, such that when administered to a subject suffering from or at risk of suffering from a disorder in which TNF α activity is detrimental, the disorder is treated. In one embodiment, a TNF α inhibitor is a compound, excluding etanercept and infliximab, which inhibits TNF α activity. In another embodiment, the TNF α inhibitors of the invention are used to treat a TNF α -related disorder, as described in more detail in section II. In one embodiment, the TNF α inhibitor, excluding etanercept and infliximab, is used to treat a TNF α -related disorder. In another embodiment, the TNF α inhibitor, excluding etanercept and infliximab, is used to treat ankylosing spondylitis. The term also includes each of the anti- TNF α human antibodies and antibody portions described herein as well as those described in U.S. Patent Nos. 6,090,382; 6,258,562; 6,509,015; 7223,394, and in U.S. Patent Application Serial No. 10/302,356 (now abandoned), ~~and in U.S. Patent Application Serial Nos. 09/801185 and 10/302356.~~

The term "antibody", as used herein, is intended to refer to immunoglobulin molecules comprised of four polypeptide chains, two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as HCVR or VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as LCVR or VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The antibodies of the invention are described in further detail in U.S. Patent Nos. 6,090,382; 6,258,562; ~~and 6,509,015; and 7223,394, and in U.S. Patent Application Serial No. 10/302,356 (now abandoned), ~~and in U.S. Patent Application Serial Nos. 09/801185 and 10/302356~~, each of which is incorporated herein by reference in its entirety.~~

The term "antigen-binding portion" of an antibody (or simply "antibody portion"), as used herein, refers to one or more fragments of an antibody that retain the ability to specifically bind to an antigen (*e.g.*, hTNF α). It has been shown that the antigen-binding function of an antibody can be performed by fragments of a full-length antibody. Examples of binding fragments encompassed within the term "antigen-binding portion" of an antibody include (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a dAb fragment (Ward *et al.*, (1989) *Nature* 341:544-546), which consists of a VH domain; and (vi) an isolated complementarity determining region (CDR). Furthermore, although the two domains of the Fv fragment, VL and VH, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the VL and VH regions pair to form monovalent molecules (known as single chain Fv (scFv); see *e.g.*, Bird *et al.* (1988) *Science* 242:423-426; and Huston *et al.* (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883). Such single chain antibodies are also intended to be encompassed within the term "antigen-binding portion" of an antibody. Other forms of single chain antibodies, such as diabodies are also encompassed. Diabodies are bivalent, bispecific antibodies in which VH and VL domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with complementary domains of another chain and creating two antigen binding sites (see *e.g.*, Holliger, P., *et al.* (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-6448; Poljak, R.J., *et al.* (1994) *Structure* 2:1121-1123). The antibody portions of the invention are described in further detail in U.S. Patent Nos. 6,090,382, 6,258,562, 6,258,562; and 6,509,015; and 7,223,394, and in U.S. Patent Application Serial No. 10/302,356 (now abandoned), and in U.S. Patent Application Serial Nos. 09/801,185 and 10/302,356, each of which is incorporated herein by reference in its entirety.